Case Report

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Effectiveness of endoscopic transsphenoidal surgery for gonadotroph adenoma mimicking dementia: A case report

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Summary **There are few reports of pituitary adenomas (PA) mimicking dementia. Delay in disease diagnosis and treatment may result in poor clinical outcome. We experienced a rare case where endoscopic transsphenoidal surgery (eTSS) effectively treated a gonadotroph adenoma mimicking dementia and report on literature considerations. We report the case of a 72-year-old man with chief complaints of cognitive decline, bradykinesia, anorexia, dressing apraxia, and vigor decline over several months. He was admitted to our hospital for scrutiny in a disoriented state. Blood tests showed hyponatremia and thyroid hormone depression. Magnetic resonance imaging showed a pituitary tumor, and preoperative endocrine stress tests showed reduced reactivities of growth hormone, adrenocorticotropic hormone/cortisol, and luteinizing hormone/follicle-stimulating hormone. Symptomatic pituitary adenoma was suspected, and eTSS was performed. The permanent pathological diagnosis was of gonadotroph adenoma. Postoperatively, the hyponatremia, cognitive decline, movement retardation, loss of appetite, dressing apraxia, and limb edema markedly improved. The patient was discharged under hydrocortisone 15 mg/day administration without complications. The endocrine stress test performed 2 months postoperatively showed secondary hypoadrenocorticism, while the other endocrine functions had normalized. No recurrence had occurred by 30 months postoperatively; the medication of hydrocortisone was gradually discontinued and the patient at the time was still being followed as an outpatient with modified Rankin Scale score 0. Secondary hypothyroidism and secondary hypoadrenocorticism due to the pituitary tumor primarily caused the condition. It is important to consider PA in the differential diagnosis of dementia, and early diagnosis and treatment can contribute to a patient's good clinical outcome.**

Keywords: Pituitary adenoma, endoscopic transsphenoidal surgery, dementia, hypoadrenocorticism, cognitive decline

1. Introduction

There are few reports of pituitary adenomas (PAs) mimicking dementia, *e.g*., Brisman *et al*. (*1*) reported a case of reversible dementia due to macroprolactinoma. The case involved a patient with a huge prolactinoma who came to medical attention because of dementia. The tumor shrank dramatically after bromocriptine therapy, and the patient's mental status returned to normal (*1*). Subfrontal tumors are an infrequent cause of dementia (*1*). A giant pituitary adenoma can be easily identified as a cause of dementia, but it may be overlooked if it is a localized lesion in the sella.

Delay in disease diagnosis and treatment may result in poor clinical outcome. We experienced a rare case where endoscopic transsphenoidal surgery (eTSS) effectively treated a gonadotroph adenoma, at the localized sellar lesion, mimicking dementia and report

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on literature considerations.

2. Case Report

A 72-year-old man with chief complaints of cognitive decline, bradykinesia, slow thinking, anorexia, dressing apraxia, and vigor decline over several months and past history of hypertension and dyslipidemia was admitted to our hospital for scrutiny. On admission, he was disoriented and had a blood pressure and body temperature of 110/62 mmHg and 36.2 °C, respectively. His height was 170 cm, and his weight was 64.5 kg. His heart and respiratory sounds were normal and he had no neurological deficits; his heart rate was 62 beats/min. Blood tests showed hyponatremia (Na, 127 mEq/L) and cortisol depression (adrenocorticotropic hormone (ACTH), 9.3 pg/mL; cortisol, 0.69 μg/dL) and thyroid hormone depression (thyroid-stimulating hormone (TSH), 1.78 ng/mL; free thyroxine, 0.78 ng/mL; free triiodothyronine, 2.22 ng/mL) were noted. We performed head magnetic resonance imaging (MRI) to investigate the dementia symptoms and detected a pituitary tumor (maximum size, 18 mm), with a strengthened signal on gadolinium (Gd)-T1-weighted imaging (Figure 1).

The blood and endocrine test results are outlined in Table 1, which shows that there were reduced reactivities of ACTH/cortisol and luteinizing hormone/follicle-stimulating hormone (LH/FSH).

2.1. *Preoperative endocrine tolerance test*

The corticotropin-releasing hormone (CRH) loading test revealed reduced reactivity of ACTH/cortisol and growth hormone (GH). The thyroid releasing hormone (TRH) loading test showed normal reactivity of TSH and reduced reactivity of GH. The LH-releasing hormone (LH-RH) loading test showed reduced reactivities of LH/FSH. The growth hormone releasing peptide-2 loading test showed normal reactivity of GH and prolactin.

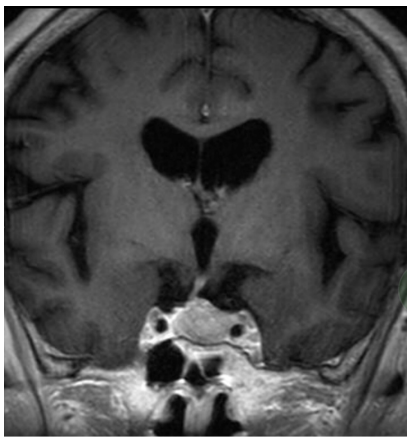

Figure 1. Head gadolinium-T1-weighted magnetic resonance imaging at first visit shows a pituitary tumor in the sella.

2.2. *Hospitalization course*

Symptomatic PA was suspected, and eTSS was performed. After incising the dura mater at the bottom of the sella, extracapsular extraction was performed, and gross total resection was achieved. No cerebrospinal fluid leakage was observed during the eTSS, and the surgery was completed after reconstruction of the bottom of the sella. Permanent pathology revealed a gonadotroph adenoma, and immunohistology revealed LH/FSH-positive intracellular staining (Figure 2).

2.3. *Postoperative course*

Postoperatively, we did not observe recurrence of the tumorous lesion on MRI (Figure 3). There were no

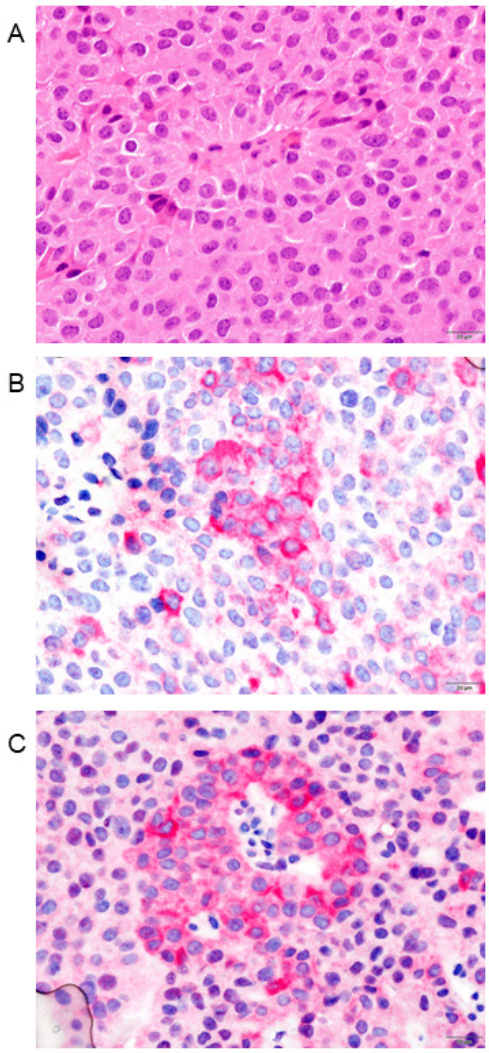

Figure 2. Permanent pathology reveals a gonadotroph adenoma (A; hematoxylin and eosin stain; H&E×60), and immunohistology reveals luteinizing hormone (B; ×60) / follicle-stimulating hormone (C; ×60) -positive intracellular staining.

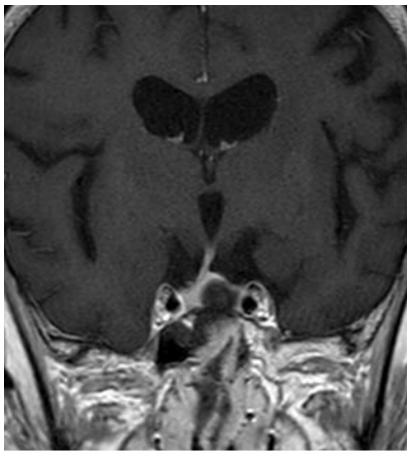

Figure 3. Postoperative gadolinium-T1 magnetic resonance imaging shows no tumor.

complications, such as cerebrospinal fluid leakage or diabetes insipidus. The patient's hyponatremia, cognitive decline, movement retardation, loss of appetite, dressing apraxia, and edema of the limbs markedly improved. The patient was prescribed hydrocortisone (15 mg/day) and was discharged. Two months postoperatively, he underwent an endocrine tolerance test. The CRH loading test showed normal reactivity of ACTH and reduced reactivity of cortisol. The TRH loading test showed normal reactivity of TSH. The LH-RH loading tests showed reduced reactivities of LH/FSH, while the baseline levels of LH/FSH had improved to the normal levels compared to the preoperative values. All other test results were normal. No recurrence was observed within the first 14 postoperative months, and the ACTH/cortisol secretion abilities were found to have improved; the oral administration of hydrocortisone was gradually discontinued. At 30 months after eTSS, he was being followed as an outpatient with modified Rankin Scale score 0.

3. Discussion

This may first appear as a case where a pituitary tumor was accidentally discovered by close examination of cognitive symptoms, but the principal symptoms were caused by hormonal disorder; therefore, the case does not fit the definition of pituitary incidentaloma (*2-4*). Aszalós (*5*) reported that the connection between the central nervous system and the endocrine system is extremely complex. The hypothalamus serves as a crucial center for the integration and coordination of autonomic functions by neuronal and hormonal pathways. It plays a central role in the homeostatic regulation of internal physiological conditions. It controls growth and reproduction, stress reactions, and determines rhythmicity, periodicity, and timing of physiological processes. CRH acts as a neurotransmitter; it has a special role in stress-behavior, anxiety, and depression and it blocks deep sleep. The most characteristic neurological sign of PA is the visual field defect. The main psychiatric symptom of hypopituitarism is a combination of dementia and delirium (*5*).

Benvenga (*6*) *et al*. reported that central hypothyroidism (CH) is a rare cause of hypothyroidism. CH is frequently overlooked, as its clinical picture is subtle and includes non-specific symptoms; furthermore, if measurement of TSH alone is used to screen for thyroid function, TSH concentrations can be normal or even above the upper normal reference limit. Indeed, certain patients are at risk of developing CH, such as those with a pituitary adenoma or hypophysitis, those who have been treated for a childhood malignancy, have suffered a head trauma, sub-arachnoid hemorrhage or meningitis, and those who are using drugs capable of reducing TSH secretion (*6*). Adult-onset CH, as is the case in primary hypothyroidism, involves symptoms such as lethargy, fatigue, eyelid edema, feeling cold, weight gain, bradykinesia, lethargy, memory loss, constipation, and crying. However, caution is required because these symptoms may be suppressed by other hormone-producing tumor symptoms or symptoms of anterior pituitary hormone secretion deficiency. Particularly when the ACTH/cortisol functions are disordered, hypofunction-associated consciousness disturbance may ensue; hence, it is challenging to distinguish the symptoms of hypothyroidism (*7*). In addition, hypogonadism, GH deficiency, and diabetes insipidus may be recognized simultaneously, which may render diagnosis difficult.

In our case, the patient was diagnosed with CH and secondary hypoadrenocorticism, caused by an otherwise normal pituitary being compressed by the tumor, based on the clinical course, imaging findings, and endocrinological examination. A PubMed search showed that this is the first diagnosed case of a gonadotroph adenoma mimicking dementia. Early diagnosis and treatment of this case resulted in complete remission, and we plan to follow the patient in the long term.

In conclusion, we reported the rare case of a patient with a gonadotroph adenoma mimicking dementia. Secondary hypothyroidism and secondary hypoadrenocorticism due to tumor, primarily caused the condition. It is important to consider PA in the differential diagnosis of dementia, and early diagnosis and treatment can contribute to a patient's good clinical outcome.

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